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Isostearyl Mixed Anhydrides for the Preparation of N-Methylated Peptides Using C-Terminally Unprotected N-Methylamino Acids
Org. Lett. **2020**, 22, 8039–8043, DOI: 10.1021/acs.orglett.0c02984.

Anhydride-Mediated Peptide Synthesis with C-Terminal Unprotected *N*-Methylamino Acids

94% yield, > 99.9% ee

86% yield, dr > 99.5:0.5

96% yield, dr > 99.5:0.5

97% yield, dr > 99.5:0.5

76% yield, dr > 99.5:0.5

96% yield, dr > 99.5:0.5

77% yield, dr^a > 99.5:0.5

91% yield, dr > 99.5:0.5

93% yield, dr^a = 98.6:1.4

^a Coupling reaction was conducted at 60 °C.

Significance: The synthesis of N-methylated peptides is an important field in organic chemistry and medicinal chemistry. The authors used isostearic acid bromide to generate mixed anhydrides to react with C-terminal-unprotected *N*-methylamino acids to prepare N-methylated peptides with the assistance of a silylation reagent.

Comment: Various N-methylated peptides were prepared through the mixed anhydrides intermediate. The reaction proceeds under mild conditions, and the yields of the desired products are good to excellent.

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Category

Peptide Chemistry

Key words

mixed anhydrides

silylation reagent

***N*-methylamino acids**

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